

Contribution of Radon and Radon Daughters to Respiratory Cancer

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This article reviews studies on the contribution of radon and radon daughters to respiratory cancer and proposes recommendations for further research, particularly a national radon survey. The steady-state outdoor radon concentration averages 200 pCi/m³, and indoor levels are about 4 times higher. The primary source of radon in homes is the underlying soil; entry depends on multiple variables and reduced ventilation for energy conservation increases indoor radon levels. Occupational exposures are expressed in units of radon daughter potential energy concentration or working level (WL). Cumulative exposure is the product of the working level and the time exposed. The unit for cumulative exposure is the working level month (WLM). The occupational standard for radon exposure is 4 WLM/year, and 2 WLM/year has been suggested as a guideline for remedial action in homes. Epidemiologic studies show that miners with cumulative radon daughter exposures somewhat below 100 WLM have excess lung cancer mortality. Some 3% to 8% of miners studied have developed lung cancer attributable to radon daughters. All of the underground mining studies show an increased risk of lung cancer with radon daughter exposure. All cell types of lung cancer increased with radon exposure. If radon and smoking act in a multiplicative manner, then the risk for smokers could be 10 times that for nonsmokers. The potential risk of lung cancer appears to be between 1 and 2 per 10,000/WLM, which yields a significant number of lung cancers as some 220 million persons in the United States are exposed on average to 10 to 20 WLM/lifetime.

Human Exposure

Everyone is continuously exposed to radon and its radioactive daughters. All rocks and soils contain the primordial series headed by uranium-238 ($t_{1/2} = 4.5 \times 10^9$ years), and the fifth member of the series, radium, decays to gaseous radon ($t_{1/2} = 3.8$ days). Average soil contains about 1 pCi radium/g, and this concentration supports an average soil surface emanation rate of 0.5 pCi radon/m²sec. This emanation rate produces a steady state outdoor radon concentration that averages 200 pCi/m³. Indoor concentrations, because of the absence of dilution capacity of the outdoor atmosphere, are about 4 times higher. Radon in groundwater can attain very high levels and add to the indoor exposure appreciably (1,2).

Occupational exposures are generally expressed in

units of radon daughter potential energy concentration or working level (WL).^{*} Cumulative exposure is expressed as the working level month (WLM) and is exposure rate multiplied by time in units of the work month.

Historically, the working level month was thought to be proportional to lung dose. Also, it is an easy measurement to perform, requiring only a single alpha measurement on an air-sampling filter. In either mines or homes, a rough equivalence of air radon concentration and WL is that 1 pCi radon/L is equal to 0.005 WL. Since average indoor environmental exposure is perhaps 0.8 pCi radon/L (0.004 WL), this is equivalent to an exposure of 0.2 WLM/year (3). The uranium content of mined ores can be many thousands of times normal soil values, and in the past, occupational exposures of hundreds of WLM/year were not unknown in the exposure cohorts studied.

In the United States, the occupational standard was reduced from 12 WLM/year to 4 WLM/year in 1971. In 1984, the National Council on Radiation Protection and

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*The working level was defined specifically for occupational exposure as any combination of short-lived daughters in one liter of air that will result in the emission of 1.3×10^6 MeV of potential alpha energy. The working level month is the product of working level and time in units of the 170-hr work month: WLM = (WL) (hours exposed)/170.

Measurements recommended that an environmental exposure of 2 WLM/year be used as a guideline for consideration of remedial action in the home (4). The state of Pennsylvania has adopted an action level for homes of 1 WLM/year. Canada has a remedial action level for radon contamination arising from the nuclear industry of 1 WLM/year; more complex standards are based on dose for natural radon in homes. Sweden requires remedial action in homes if the level is greater than 5 WLM/year.

Data on exposures to environmental radon and the distribution of the exposure data are scant. Based on few measurements, it was assumed by NCRP (4) that exposure distribution in the United States is lognormal and that the average exposure could be 0.2 WLM/year (median 0.14), with a geometric standard deviation of about 2.5. If these assumptions are correct, then 0.14% of the U.S. population is exposed to 2 WLM/year or greater from natural sources. About 10 times as many people would be exposed to 1 WLM/year or greater.

The source of radon in homes is primarily the soil underneath the dwelling. However, for similar soil radium content, indoor radon concentrations can vary over several orders of magnitude. Radon entry depends upon the house-to-soil coupling, soil moisture, and indoor-outdoor pressure differences, among other variables. Attempts to reduce ventilation for energy conservation undoubtedly increase indoor radon levels.

Respiratory Cancer

In most of the large epidemiologic studies conducted to date, miners with cumulative radon daughter exposures somewhat below 100 WLM have excess lung cancer mortality. There are four major studies in which a dose-response can be inferred (5-10). These include 3362 U.S. underground uranium miners followed since 1950 whose exposures range from 60 to 7000 WLM (average 800); 15,984 Canadian uranium miners with upper estimate exposures ranging from 5 to 510 WLM (average 74); 2400 Czechoslovakian miners followed since 1948 with an exposure range from 72 to 716 WLM (average 200); and 1415 Swedish iron miners born between 1880 and 1919 who were alive in 1930 and exposed to 27 to 218 WLM (average 80). To date, from 3% to 8% of the miners studied have developed lung cancer attributable to radon daughters (above that expected from smoking or other causes alone).

Most lung cancer is bronchogenic, a fact that did considerable damage to the appropriateness of the WL and WLM as exposure units. The potential alpha energy in air is proportional to whole lung dose but not directly proportional to bronchial dose because aerosol characteristics must be considered. It is the short-lived daughters of radon (^{218}Po and ^{214}Po), which arise through decay of radon, that actually deposit on the bronchial airways and deliver the carcinogenic dose. Most of the short-lived daughters attach to the natural aerosol, but a few percent of the first daughter, ^{218}Po , remains unattached to the natural aerosol. Its small size allows

efficient (100%) deposition in the upper airways and about 30% of the total alpha dose is due to the unattached ^{218}Po . Only a small fraction of the inhaled radon daughters deposit on the bronchial tree, and bronchial dose must be modeled from airway dimensions. In addition, the bronchial dose from ^{218}Po not attached to aerosol particles is greater than that from ^{218}Po attached to aerosols and that was not considered in defining WL.

The cell type of the bronchogenic carcinoma does not define the lung cancer etiology. Small cell or oat cell carcinoma is the earliest to appear, but all forms are increased by radon daughter exposure. In underground miners with the longest latent intervals, epidermoid carcinoma appeared dominant. The tumor cell type has been shown to vary with many parameters, including smoking quantity, age at first underground exposure, and latent interval. The percentage of small cell carcinoma decreased, and the percentage of epidermoid carcinoma increased with latent interval (11). In view of the numerous cell types involved, documenting etiology by type seems unlikely.

Special Groups

Certain individuals or groups could be more or less sensitive to the effects of ionizing radiation from radon daughters. Smokers or individuals with pulmonary disease may be more affected because of stimulation of cell division in the bronchial tree (promotional effects of the irritant). Nonsmokers may be less sensitive. The underlying model for the appearance of tumors following exposure has an important bearing upon the response of specific groups; however, the model for the time course of lung cancer development following radon daughter exposure is not known. The cohorts under study will not go to closure for perhaps another 20 years.

The types of models that have been used for risk projection have generally followed either an absolute or a relative risk model. Lung cancer rarely appears before age 40, regardless of age at exposure, and never before a minimum latent interval following exposure of 5 to 10 years. Most absolute models are modified to include these basic features and an average annual rate of appearance. One model decreases the annual rate of appearance following each exposure with an empirical exponential correction (3). Another model increases the annual rate of appearance as age of exposure increases (6). The relative risk model increases the "natural disease incidence" by a constant fraction (risk coefficient) per WLM (12,13).

In a relative risk model, lifetime risk from radon daughter exposure is directly proportional to the natural appearance of lung cancer. Nonsmokers have approximately one-tenth the lung cancer rate of smokers, and nonsmoking women have a lower rate than nonsmoking men. Thus, radon daughter-related lung cancer could be dependent upon sex, life span (which leads to overall higher lifetime lung cancer risk), and smoking history.

If average levels of radon daughters induce a significant fraction of the natural incidence of the disease in nonsmokers, then the pure risk of disease in the absence of radon must be reevaluated and different relative risk coefficients estimated.

A modified absolute risk model could accommodate specific groups by varying the risk coefficient. Not enough is known concerning the validity of the various models to take a stand with regard to the use of a particular model applied to specific groups. It is also possible that no proposed model will adequately describe the data.

From a dosimetric viewpoint, children about 10 years old have twice the bronchial dose per unit exposure as adults (3). This is due to their small lung dimensions along with almost equivalent minute volumes. Adults with small lung dimensions also receive a higher bronchial alpha dose per unit exposure, and therefore their risk is higher by a factor that can be estimated given the bronchial morphometry.

Interactions with Other Pollutants

If exposure to radon increases the risk in a multiplicative manner, then whatever other factors influence lung cancer rates must directly influence radon daughter-related lung cancer. The most important pollutant or factor is cigarette smoke. If smoking and radiation interact multiplicatively, the effect of radon daughters might be 10-fold higher for smokers than for nonsmokers. However, available data from the Swedish underground iron miner cohort appear to support an additive model rather than a multiplicative model. The response to external gamma ray radiation exposure for lung cancer in Japanese atomic bomb survivors also appears to support an additive effect when smokers and nonsmokers are compared (14). Samet et al. observed a larger relative risk in Navajo uranium miners (primarily nonsmokers) than would be expected in smoking white miners (15). This implies an additive effect. The Whittemore and McMillan model, on the other hand, predicts a fixed relative risk coefficient for any given risk for smoking (13).

Risk Assessment

Risk projection models have been developed to estimate lifetime risk to the mining populations and for environmental exposures. The range for most models lies between 1 and 4 lung cancers per 10,000 persons exposed per WLM. A plausible range for environmental exposures at the 10 to 20 WLM lifetime exposure level is from 0 (if a threshold exists) to 5 per 10,000 per WLM (if all environmental lung cancer is radon daughter-related). When calculating an incremental risk due to increased environmental exposure, for example, the age at exposure should be considered. A person aged 60, if exposed to an elevated radon daughter level for the remainder of life (on average 24 years), will have a lower risk than an individual aged 30 exposed similarly for 24

years because of the potential for more years of risk expression. NCRP has developed tables that allow age at exposure to be considered (3). In general, except for those over 60, the risk appears to be between 1 and 2 per 10,000 per WLM. Although this is a small risk, the large number of persons exposed in the United States (220 million persons exposed to 10 to 20 WLM lifetime) yields a significant number of lung cancers.

Muller (private communication) believes that pooling of the U.S. and Canadian underground miner data for further analysis would yield better lifetime risk estimates. It should be emphasized that lifetime risk is the most important and useful concept because of the continuous nature of exposure throughout life.

Studies with experimental animals have generally been supportive of the human epidemiology. The risk estimates per unit exposure, primarily for rats, with some confirmation from dogs, are similar to those for humans (1,3). These studies have helped to clarify many of the uncertainties in the epidemiologic studies regarding the roles of radon daughter exposure rate, disequilibrium, and unattached fraction, as well as cigarette smoke, diesel exhaust, and ore dust exposures.

The following recommendations are proposed as the key elements in apportioning environmentally induced radon lung cancer.

Research Recommendations

Recommendation 1: A national radon survey should be conducted. Data on the concentration of radon in air and water in homes in the United States have been collected in small surveys done for special purposes. A systematic national survey is needed to determine an accurate average radon exposure and the distribution of exposure. A systematic survey will also locate geologic areas of high radon exposure that would not be detected by the special purpose surveys. Inexpensive measurement techniques are available. This survey could be combined with existing health data collection of the National Health Interview Survey or the National Health and Nutrition Examination Survey, and such a combination would result in substantial savings in travel and questionnaire expense. This would allow the linkage of the radon data with other health data for smoking and health consequences and permit a risk assessment for lung cancer.

The quality of many past data sets involving radon or radon daughter measurements is discouraging. Any study of nationwide levels of indoor radon concentrations should be accompanied by quality assurance data indicating that the measurements accurately represent exposure. Much past information on indoor radon concentrations provides little more than screening information and cannot be used for scientific purposes.

From 10% to 20% of all measurements should be devoted to quality assurance information. These samples would be in the form of blind duplicates, positive controls, and blanks. Data from any study that does not

provide quality assurance should not be included in the nationwide survey.

Calibration and quality control can be performed, for example, at the Eastern Environmental Measurement Laboratory of the U.S. Environmental Protection Agency (EPA) in Montgomery, Alabama. Some measurements for radon in water use radium standards from the U.S. EPA Las Vegas Laboratory. Radon in air measurements can be validated using radon chambers at the U.S. Department of Energy Environmental Measurement Laboratory in New York City.

Recommendation 2: Improved epidemiologic information should be obtained through international pooling of data. Many issues relevant to assessing the risks associated with radon daughter exposures are still unresolved because the appropriate analyses have not been carried out, the necessary data are not available in a particular study, or different studies appear to have produced different results. These include the shape and magnitude of the dose-response relationship and its modification by exposure to other agents (notably smoking), time-related factors such as age at exposure, and insufficient data or errors of exposure measurement. For many of these issues, the necessary data have already been collected at considerable expense, and the appropriate analyses could be carried out at relatively modest additional cost. These raw data, together with the necessary funding, should be made available to an appropriate team of investigators to undertake these analyses on a systematic basis.

Certain of these questions might be better addressed by one data set or another, whereas others would require comparison and/or pooling of more than one data set. Where data sets truly are comparable, a substantial improvement in statistical power can result from pooling, allowing questions to be answered that no single study could address. Furthermore, apparent discrepancies can be resolved only by adoption of a consistent methodology and careful analysis of modifying factors that differ between studies. Finally, comparison over a range of exposure levels or modifying conditions can be strengthened by pooling data sets with contrasting distributions of such factors. We recommend that, as a first step in this direction, the Colorado Plateau and Ontario uranium miner data be pooled and that efforts be made to identify other data sets that would also be suitable for this purpose.

These analyses should also include a reevaluation of the risk assessment for radon daughters. The results of such a study could be used as a basis for standard setting for radon and its progeny in the workplace—notably mines—and with appropriate reservations, an extrapolation of derived risk factors to residential exposures could be made.

Recommendation 3: Epidemiologic studies of miners that are in progress should be continued, and new populations should be studied, if justified by the exposure pattern. Studies of uranium and other underground miners exposed to radon daughters have been the principal source of human data on lung cancer risks from

inhalation. These longitudinal studies should be maintained, particularly to attain lifetime followup of the younger subjects. Any new mining populations with high exposures to radon daughters should be enrolled in a prospective study.

Recommendation 4: Experimental animal studies should be conducted. Human risk factors for radon daughter exposure are poorly known and exist only for adult male underground miners. These miners are also exposed to long-lived radioactive dusts, diesel exhaust, cigarette smoke, other pollutants associated with the host rock being mined, and external gamma radiation. Thus, the lung cancer risk factors presently used for humans represent a composite response to other factors as well as to radon daughters. Proper extrapolation of miner data for estimation of lifetime risks to populations from environmental radon daughter exposures requires experimental data on factors that modify risk, such as radon daughter exposure rate; unattachment fraction and disequilibrium; age; sex; duration of exposure; age of expression of excess risk; genetic constitution or susceptibility to carcinoma induction; and the interaction of radon daughters with other environmental pollutants, including any influence of the temporal sequencing of co-pollutant exposures. These elements of the problem must be studied in animals, and the funding of such studies should be encouraged.

The development of biological multistage models of radiation carcinogenesis and the incorporation of the oncogene work into statistical models are necessary for clarification of the basic biology of radiogenic and non-radiogenic tumors. Oncogene models offer the potential for distinguishing radiogenic tumors from nonradiogenic tumors and, therefore, are potential tools of molecular biology.

Recommendation 5: A personal dosimeter for occupational radon exposure should be developed. The most serious fault in all follow-up studies of underground miners (which form the basis of risk projection models) is the poor quality or lack of radon daughter exposure measurements. This is well known, yet no attempt to provide reliable exposure estimates in any future studies has been initiated. An inexpensive, passive, reliable integrating radon monitor should be developed and tested, which would provide the high-quality data needed. The monitor would be used by every individual exposed occupationally, with strict quality control measures, to provide exposure data. Existing protocols of point measurements would not be superseded but would be supplemented by the personal monitor data. Combined data could provide information that bears on the relationship between the weighted exposures, as previously and currently estimated from point measurements, and actual individual measurements. The point measurements are also needed to provide information on radon-to-radon daughter ratios, which, although fairly constant, must be known in order to infer alpha dose.

A consideration of future occupational exposure should also require that the unattached fraction of radon

daughters be measured. The point measurements performed in mines should be modified to provide these data.

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